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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,163	02/20/2002	Susanna Chubinskaya	STK-081	8382

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EXAMINER	
COUNTS, GARY W	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 01/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,163	CHUBINSKAYA ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *1-8,10-16,22,24-32,35-43 and 45-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,17-21,23,33,34 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 11/05/02, 01/06/03, 03/04/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group V, Claims 9, 17-21, 23, 33, 34 and 44 in the reply filed on October 29, 2004 is acknowledged. The traversal is on the ground(s) that the claims of Groups I, III, V, and IX are directed to diagnostic methods for determining the presence or severity of a disease affecting a joint that require determining OP-1 protein levels in patient tissue samples and that Groups I, III, V and IX all belong to class 435. Applicant further argues that different fields of search are not required because all of these groups require analyzing OP-1 protein level. This is not found persuasive because of reasons of record and further because although Groups I, III, V and IX all belong to class 435, each of the Groups is classified into a different subclass. Applicant further argues that the claimed diagnostic methods are clearly capable of use together and do not have different effects in different patient populations. This is not found persuasive because as stated in the previous office action the methods would have different subpopulations of patients. As disclosed by Applicant in the specification on page 13, line 28 – page 14, line 8. Different predetermined standards and standard values are used with the different methods. Therefore the search for the different groups requires different search terms and a different search strategy that creates a burden on the examiner. Further, while searches would be expected to overlap, there is no reason to expect the searches to be coextensive.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

3. Claims 9, 17-21, 23, 33, 34 and 44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re W*ands USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to a method of determining the presence of an age-related tissue disorder in a patient, the method comprising determining an amount of OP-1 protein present in a joint tissue sample from the patient; and comparing the amount of OP-1 protein present in the sample and the predetermined standard is indicative of an age-related tissue disorder.

The specification fails to properly provide adequate written description to enable the methods as claimed. The specification on page 16, lines 19-23 discloses that OP-1 protein levels can be an indicia of tissue integrity or health but not necessarily an indicia of an underlying cause of tissue deterioration or ill-health. For example, OP-1 is an indicia of cartilage degeneration which accompanies inflammatory joint disease as well as an indicia of age-related cartilage deterioration which is independent of disease. The specification on page 11, lines 19-24 disclose that OP-1 protein levels decrease as a consequence of normal aging and in response to inflammation. OP-1 protein levels in cartilage decrease with increasing age of a patient regardless of the presence of observable cartilage degradation. The specification on page 6 discloses that inflammation can be caused by autoimmune disease. The specification on pages 25 and 26 discloses that such things as gout, fibromyalgea syndrome (FMS and polymyalgea rheumatica (PMR) cause a decrease in OP-protein.

The working examples are directed to determining a decrease in OP-1 protein. The specification on page 23, lines 1-11 discloses the content of endogenous OP-1 protein significantly decreased with increased age. The specification on page 26, lines 8-12 discloses that a marked decrease in OP-1 protein in OA and RA patients.

The specification only teaches decreased levels of OP-1 as age increases and teaches multiple causations for decreased OP-1 levels. The specification does not provide guidance on how to distinguish between age or osteoarthritis or rheumatoid arthritis or gout or FMS or PMR. The specification does not provide any guidance for using these levels to positively determine an age-related tissue disorder. For example, if the sample is taken from an individual and a decreased level of OP-1 is determined as compared to a normal standard.

How can one skilled in the art determine if it is age related or related to inflammation? Furthermore, it is unclear what is considered to be an age-related tissue disorder, as recited in the instant claims (see 112 2nd rejection). Such is not seen as sufficient to support the breath of the claims and one skilled in the art cannot practice the claimed invention without undue experimentation, because in order to positively determine the presence of an age-related tissue disorder, one skilled in the art would have to be able to distinguish age from inflammation.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

5. Claims 9, 17-21, 23, 33, 34 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is vague and indefinite because it is unclear what is the intended scope of the claim. It is unclear what is considered to be an age-related tissue disorder.

Claim 9 is vague and indefinite because of the recitation " a difference in the amount of OP-1 protein". It is unclear what difference applicant is referring to. Does applicant intend and increase or a decrease in the amount? The specification on page 11 discloses that OP-1 protein levels decrease as a consequence of normal aging and in response to inflammation.

Conclusion

6. No claims are allowed.

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Findlay et al. (WO 00/13024) disclose the level of markers such as BMP-7 (OP-1) as a predictive measure of the potential for onset of a severe form of certain skeletal disorders. Findlay et al disclose taking a sample of body tissue or body fluid and measuring the level of the marker in the sample and comparing the level to a standard to determine whether the level of the marker falls within a range indicative of a potential of the individual to progress to exhibit overt symptoms of the disorder. Findlay et al disclose that the sample can be any body fluid in which regulators or markers or bone remodeling are found. Findlay et al disclose that the skeletal disorder can be osteoarthritis or osteoporosis.

Jones et al., (WO 94/03600) disclose determining OP-1 in a body fluid by ELISA protocol.

Flechtenmacher et al (Arthritis & Rheumatism, Vol 39, No. 11 1996) disclose that Recombinant OP-1 is a potent stimulator of the synthesis of cartilage-specific matrix macromolecules by human reticular chondrocytes.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts
Examiner
Art Unit 1641
December 29, 2004

LONG V. LE
SUPERVISORY PATENT EXAMINER
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1/7/04